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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/513,086	02/24/00	MANSFIELD L	MSU 4.1-458

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HM12/0815

EXAMINER
WOITACH, J

ART UNIT	PAPER NUMBER
1632	10

DATE MAILED: 08/15/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/513,086	MANSFIELD ET AL.	
	Examiner	Art Unit	
	Joseph Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-9,13-17,23-28,45,46,49 and 50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-9,13-17,23-28,45,46,49 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 7, 2001 has been entered.

Applicants amendment filed May 7, 2001, paper number 9, has been received and entered. The specification has been amended. Claims 1-3, 10-12, 18-22, 29-44 and 47-48 have been canceled. Claims 4 and 23 have been amended. Claims 4-9, 13-17, 23-28, 45-46, 49 and 50 are pending and currently under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-9, 13-17, 23-28, 45-46, 49 and 50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way

as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

The claims encompass a vaccine comprising at least one epitope of a recombinant polypeptide consist of one epitope of a 16(±4) kDa antigen and one epitope of a 30(±4) kDa antigen and methods of making said recombinant protein. Review of the present specification, the art of record, and a search of the sequence databases for polypeptide and polynucleotide sequences for the epitope of the 16(±4) kDa antigen and the 30(±4) kDa antigen indicates that these sequences have not been identified nor described. Presently, in order to practice the invention as claimed the artisan must first obtain the polypeptide and/or polynucleotide sequences of the 16(±4) kDa antigen and the 30(±4) kDa antigen. The specification describes general methods of cloning cDNA sequences from expression libraries, however, the sequences obtained by this method are not disclosed. The specification fails to provide any detail to any of the sequences of the 16(±4) kDa antigen or the 30(±4) kDa antigen. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not

adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998). In the instant case, the claimed embodiments of the polypeptide and polynucleotide sequences needed to make and use the invention as claimed lack a written description. The specification fails to describe any polynucleotides or polypeptides encompassed in the claims with particularity to indicate that Applicants had possession of the claimed invention. The written description of a claim is evaluated on the basis of the claimed invention as a whole. Case law established that the requirement for written description relates to the subject matter defined by the claims. *In re Wright*, 9 USPQ2d 1649 (Fed. Cir. 1989). To this end, while antibodies exist which recognize a 16(±4) kDa antigen or a 30(±4) kDa antigen, no specific sequence which is recognized by these antibodies is disclosed. The claimed invention is directed to vaccine comprising at least one epitope of a recombinant polypeptide consist of one epitope of a 16(±4) kDa antigen and one eptitope of a 30(±4) kDa antigen and methods of making said recombinant protein, and the specification fails to demonstrate possession of the invention by actual reduction to practice. The skilled artisan cannot envision the detailed structure of the claimed vaccine, nor the materials necessary to practice the methods steps necessary to carry out the claimed methods of generating

recombinant protein which would serve as an antigen/vaccine, and thus, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Case law has established that one cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483.

The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art **as of Applicants effective filing date**. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, the polypeptide and polynucleotide sequences needed to make and use the claimed invention do meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 4-9, 13-17, 45-46, 49 and 50 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants state that the specification discloses a vaccine that contains recombinant polypeptides that comprise one or more epitopes from the 16(±4) kDa antigen and the 30(±4) kDa antigen. Applicants summarize both Kisthardt and Liang *et al.*, and argue that while results using antibodies *in vitro* indicate that antibodies are not neutralizing, this is no indication of the effectiveness of an antibody *in vivo* (Applicant's amendment, page 6). Applicant's point out that Liang *et al.* teach that despite a high exposure rate there is a relatively low incidence of clinical EPM, and that a horse infected with *S. neurona* develop antibodies to several antigens. Applicants argue that it may be plausible that antibodies to one or both of the instantly claimed antigens would be involved in preventing *S. neurona* form invading neural tissue. It is argued that historically vaccines have been developed against a variety of pathogens which have been first identified by reactivity with antisera (Applicant's amendment, pages 7-8). Further, since the 16(±4) kDa antigen and the 30(±4) kDa antigen have been identified as surface antigens and that surface antigens are generally important in the function of the organism, they may serve as targets for neutralizing antibodies (Applicant's amendment, page 9). Applicants arguments have been fully considered but not found persuasive.

First, as noted in the previous office action, Stedman's Medical Dictionary defines a vaccine as essentially any preparation intended for active immunological prophylaxis. Applicants state that the present vaccine does not prevent the *Sarcocystis neurona* from infecting the equine (page 3; first full paragraph, first line), however the claims still recite the limitation of a 'vaccine for active immunization of an equine against a *Sarcocystis neurona* infection' (claim 4). Examiner agrees with Applicants arguments that an antigen may serve as a vaccine generating neutralizing antibodies. However, in light of the teaching of Liang *et al.* it is clear that not all antibodies generated to an antigen will neutralize function of said protein. Further, Liang *et al.* teach that '[A]lthough *S. neurona* was sensitive to specific antibodies, a 10-min exposure to antiserum was required to yield a significant reduction in parasite production (data not shown). This may partially explain why protective antibodies to some apicomplexan parasites are effective *in vitro* but not *in vivo* (23). Newly released parasites are exposed to serum for a shorter time *in vivo*, and the access of neutralization-sensitive epitopes to antibody may be limited (31).' (page 1837, bottom of first column). Further, Liang *et al.* teach that cytotoxic T-cells are ineffective in attacking merozoites migrating to the central nervous system, and conclude while Sn 16 and Sn 14 are expressed *in vivo*, further investigation of these candidate antigens is necessary for inclusion in a vaccine (page 1837, bridging paragraphs of first and second columns). The results of and conclusion by Liang *et al.* clearly indicates that *in vitro* data does not necessarily correlate to or be extendable to *in vivo*. Further, Applicants admit that the present invention does not prevent infection of equine and may prevent the spread of *S. neurona* to the nervous system and

CSF. Applicants have proposed that it is plausible that the instantly claimed antigens may serve as a vaccine, however the specification does not provide evidence that the invention prevents the spread of *S. neurona* to the nervous system and CSF which support such an assertion.

The physiological art in general is acknowledged to be unpredictable (MPEP 2164.03). In light of the teachings of both Liang *et al.* and Kisthardt *et al.* demonstrating the presence of antisera reactivity in most horses tested, and the specific teaching of Liang *et al.* that the ability of an antibody to function *in vitro* does not correlate to function *in vivo,* the instant specification has not given the necessary teaching to provide a nexus between the proposed antigens and a functional prophylactic vaccine. As discussed above and the previous office action, there has not been a successful vaccine produced for *S. neurona.* The Applicants have not described nor provided examples of how the recited vaccine differs from those previously found in the art.

In addition, the polynucleotide sequences and polypeptide sequences required to practice the claimed invention are not disclosed in the instant specification, nor the art of record (discussed in detail in the 35 USC112, first paragraph- written description, rejection above). The high degree of unpredictability associated with the claimed method underscores the need to provide teachings in the specification that would provide the artisan with specific treatment regimens that achieve a therapeutic benefit; however, the specification does not provide such guidance and fails to provide the necessary guidance. In particular, none of the sequences for either the 16(±4) kDa antigen or the 30(±4) kDa antigen are disclosed. Absent this information, the artisan would not know what polypeptides or polynucleotides one would use to begin to generate the claimed

invention. Further, as indicated by Liang *et al.*, one cannot predict the activity of an antigen for use in a vaccine from *in vitro* data. While the immunological data of record strongly suggests that the antigens are cell surface antigens, there is no function ascribe to these antigens and thus, no nexus between targeting these antigens and disrupting any activity which would result in protective prophylactic effect required of a vaccine. Without necessary specific guidance in the specification and the lack of correlative working examples, the claims would require an undue amount of experimentation without a predictable degree of success on the part of the skilled artisan.

The instant invention, as claimed, falls under the "germ of an idea" concept defined by the CAFC. The court has stated that "patent protection is granted in return for an enabling disclosure, not for vague intimations of general ideas that may or may be workable". The court continues to say that "tossing out the mere germ of an idea does not constitute an enabling disclosure" and that "the specification, not knowledge in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement". (See *Genentech inc v. Novo Nordisk A/S* 42 USPQ2d 1001, at 1005). The claimed methods of transfer constitute such a "germ of an idea".

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to practice the full scope of the invention as claimed. Therefore, for the reasons above and of record, the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-9 and 23-28 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Amendments to the claims clearly defining the recombinant protein has obviated the basis of the rejection. Specifically, the amendment defining that the recombinant polypeptide consist of one epitope of a 16(±4) kDa antigen and one eptitope of a 30(±4) kDa antigen has distinguished the recombinant polypeptide from the endogenous polypeptide.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4 and 23-25 rejected under 35 U.S.C. 102(b) as being anticipated by Liang *et al.* is withdrawn.

Amendments to the claims clearly defining that the recombinant polypeptide consist of one epitope of a 16(±4) kDa antigen and one eptitope of a 30(±4) kDa antigen has distinguished the

recombinant polypeptide from the endogenous polypeptide has differentiated the claimed invention from that disclosed in Liang *et al.*

Conclusion

No claim is allowed. Claims 4-9, 13-17, 23-28, 45-46, 49 and 50 are free of the prior art of record because the art fails to teach a recombinant polypeptide consisting of one epitope of a 16(±4) kDa antigen and one eptitope of a 30(±4) kDa antigen, and use of said polypeptide as a vaccine, however the claims are subject to other rejections.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach, whose telephone number is (703) 305-3732. The examiner can normally be reached on Monday through Friday from 7:00 to 5:00 (Eastern time).

If attempts to reach the examine by telephone are unsuccessful, the examiner's supervisor, Karen M. Hauda, can be reached on (703) 305-6608.

An inquiry of a general nature or relating to the status of the application should be directed to Kay Pickney whose telephone number is (703) 305-3553.

Joseph T. Woitach

Deborah Crouch

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PRIMARY EXAMINER
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